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AN APPROACH TO THE TREATMENT OF ESSENTIAL HYPERTENSION*

The management of patients with hypertension continues to be a subject of much controversy. This paper by Dr. Samuel Proger is the first of two articles dealing with this problem. The second article, by Dr. Robert Wilkins, will appear in the November issue of MODERN CONCEPTS OF CARDIOVASCULAR DISEASE. The editors believe that the two different points of view expressed by Dr. Proger and Dr. Wilkins will be of interest to the reader. It is judged outside the scope of this publication to extend the discussion so as to represent all the varying opinions of workers in this field.

The average case of mild or moderate essential hypertension is likely to have a long, variable and unpredictable course. It is therefore difficult to measure the effectiveness of a given procedure or drug in such cases. On the other hand, the average case of severe or malignant hypertension exhibits such a relatively uniform and short course that the determination of the therapeutic effectiveness of a new approach can be made with less difficulty. It may be desirable, therefore, to limit therapeutic trials of new drugs and procedures to patients with severe or malignant hypertension because it is only in such patients that we can begin to comprehend what we are achieving.

For purposes of this discussion, a distinction is made between severe essential hypertension and malignant hypertension on the basis of the changes in the fundi. In both cases the level of the blood pressure may be equally high (diastolic pressure 130 mm Hg. or more). However, in the malignant phase of essential hypertension there is "albuminuric retinitis" of which papilledema is a constant feature (grade IV fundi according to Keith and Wagener) whereas in severe essential hypertension there is no papilledema (grade III). To be sure, the arteriolar necrosis of malignant hypertension may be present without papilledema or even without very high blood pressure for that matter. Under these circumstances it is difficult if not impossible to make a clinical diagnosis of malignant hypertension. For practical purposes papilledema may serve as a pathognomonic feature of malignant hypertension without which the diagnosis should not be made. Severe essential hypertension may, in a given patient, be "premalignant" since probably all patients with malignant hypertension pass through a stage of variable duration when they may be said to have severe essential hypertension. Severe essential hypertension may also of course persist for years and never proceed to the malignant phase with arteriolar necrosis.

Drugs which can almost regularly lower blood pressure are now available. We must, therefore, once and for all answer the question — "What does one accomplish by lowering blood pressure?" In attempting to answer this question it should be borne in mind that, in general, essential hypertension may take one of three courses. (1) It may remain more or less stationary, though rather labile, through a normal lifetime. (2) Although the elevation may be only mild or moderate, it may be complicated by cerebral, coronary, or renal vascular lesions with detectable visceral damage. (3) It may proceed to the severe or malignant phase with one of the customary serious sequellae of such phases.

What can be accomplished by therapy in these three groups? In the first group, obviously nothing can be accomplished. This is incidentally a fairly large group as indicated by Bell's data which show that about three fourths of people with essential hypertension die of diseases unrelated to the hypertension.

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In the second group one may or may not gain something by a lowering of the blood pressure depending upon whether atherosclerosis and its possible resulting visceral damage can in fact be prevented or lessened by the prophylactic lowering of the blood pressure. If it is decided that atherosclerosis and its possible after effects can be diminished by lowering blood pressure, then patients not only in group two, but also those in group one should be treated since it would be impossible to decide whether a patient belonged in one or the other group before visceral damage occurred. A therapeutic attack on patients in these groups represents an effort of enormous magnitude and should not be undertaken until there is reasonably good evidence that therapy is accomplishing enough to justify such an effort.

In group three, much can be gained by therapy, especially if the associated renal damage is not too severe. It is not feasible to treat all patients with mild or moderate essential hypertension in the hope of warding off or preventing malignant hypertension which will develop in only a very small number of these patients. Since it is impossible to determine which of the mild or moderate hypertensions will become malignant, one may have to limit therapy to patients with malignant hypertension or to those with severe essential hypertension who may be thought to be in the "premalignant" phase.

Just as one cannot predict which patient with mild or moderate essential hypertension will develop malignant hypertension, so also one cannot predict which patient with severe essential hypertension will develop malignant hypertension. However, severe essential hypertension is much less common than mild or moderate hypertension. Also severe hypertension is much more likely than mild or moderate hypertension to progress to the malignant phase. Furthermore, malignant hypertension may be said to be quite regularly preceded for variable periods of time by a very high level of blood pressure, — that is, by severe essential hypertension. Severe essential hypertension then is a fruitful area for therapeutic effort of even an intensive sort. One might conceivably be able to prevent malignant hypertension by the effective control of its precursor, severe essential hypertension. Any other attempt to prevent malignant hypertension will be impractical until there is an easy and safe method for treating benign and moderate hypertension over a period of decades.

Once malignant hypertension appears, every possible effort should be directed toward the lowering of blood pressure even at the risk of drug toxicity or surgical incapacitation. Incidentally, it is in malignant hypertension, before renal insufficiency has advanced too far, that the therapeutic benefits of sympathectomy have been most clearly established.

A principal therapeutic goal in essential hypertension would, therefore, appear to be the prevention and cure of malignant hypertension. This is a clear and unequivocal goal. Not only are all other goals vague as of today, but their prosecution does much to obscure and dilute more wisely directed efforts.

The widespread and more or less indiscriminate use of such agents as hexamethonium and apresoline in all patients with hypertension may do more harm than good. For the dangers of most hypotensive drugs are real; the benefits, at least in patients with benign essential hypertension, are highly presumptive. This is not to minimize the importance of the newer drugs since they represent significant steps forward in the approach to the medical treatment of essential hypertension and they need to be thoroughly evaluated.

One should measure the value of new drugs in essential hypertension not only in comparison with no treatment but in comparison with existing treatments. In mild and moderate essential hypertension no treatment may well prove preferable to treatment with the newer hypotensive drugs. On the other hand in severe and malignant hypertension the hypotensive drugs promise to be helpful agents. We must now determine whether this help is more than we have come to know can be provided by surgical sympathectomy. If medical and surgical treatments prove equally effective, one would then have to determine which of these treatments is less onerous. We instinctively think of medical therapy as "conservative" and surgical therapy as "radical". This attitude stems from the days when most medical therapy was either innocuous or easily and quickly beneficial and usually not recognisably toxic, while surgical therapy produced much obvious morbidity and mortality. We have reached an era when the serious or troublesome side effects of medication are commonplace whereas there is a sharply decreasing incidence of mortality and significant morbidity following surgery. We may have to reassess our concept of conservative and radical therapy as these terms relate to medicine versus surgery. Thus, it is quite conceivable that a simple supradiaphragmatic splanchnicectomy (Peet operation) may prove to be a more conservative method of treating hypertension than the life-long parenteral use of hexamethonium which incurs a constant need for supervision and an ever present threat of undesirable and possibly harmful side effects.

In judging the comparative value of treatments only mortality figures offer unequivocal and firm

support. If changes in blood pressure are not ultimately reflected in altered mortality rates, then the blood pressure changes are less critically important. The mortality rates to which I have reference are those specifically and directly related to the hypertension, namely those due to brain hemorrhage, left ventricular failure in the absence of recognizable coronary disease and the renal insufficiency of the severe or malignant phases of essential hypertension. It is said that only about ten per cent of patients with essential hypertension benefit significantly from surgical sympathectomy. Yet in malignant hypertension the two-year mortality rate has been reduced by surgical sympathectomy from ninety per cent or more to some fifty per cent. One may say, therefore, that at least in malignant hypertension, forty or more patients of every hundred will benefit from surgical sympathectomy. The improved mortality rate incidentally is not specifically related to a lowering of blood pressure, suggesting that sympathectomy may produce some of its benefits by means other than the lowering of blood pressure.

It is probable that vasomotor control is not a factor of major or specific significance in the problem of essential hypertension. In any event the benefits resulting from the attack on this factor are small, so small indeed as to suggest that therapeutic efforts might more profitably be directed along other lines. However, until such a time as sympathectomy, either medical or surgical, is supplanted by more specifically corrective therapy, we need to decide how best to achieve that small segment of therapeutic benefit that control of the vasomotor factor provides. In this regard the available data on mortality rates indicate that the less extensive surgical sympathectomies may be as effective as the more extensive ones. If this is true, and it seems most important to determine definitely whether it is true, then the simplest effective surgical approach should become the standard surgical approach. Once such a standard surgical approach has been established, it would be necessary to measure the value of new treatments, medical or surgical, in comparison with this approach. The comparison would be not only in terms of improved mortality rates but also in terms of how much effort and risk were involved in achieving the improved mortality rates. On this basis, for example, hexamethonium would have to be considerably more beneficial than the simplest form of surgical sympathectomy to justify preferential use.

It is smugly satisfying to look back upon the practice of medicine of fifty or a hundred years ago. We like to think of those days as a dark age in medicine. It may well be that fifty or more years hence (let us hope sooner) physicians will look back upon our present gropings in that vast, still largely unexplored wilderness known as the field of hypertension, smile knowingly and say that we, too, in the mid-twentieth century are living in a dark age medically speaking. In the meantime, it behooves us, as we continue our probings, to do as little damage as possible and to remember that in patients with essential hypertension there is particular pertinence to the concept that we must not lose sight of the patient in our concern over some of his physiological maladjustments.

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The opinions and conclusions expressed herein are those of the author and do not necessarily represent the official views of the Scientific Council of the American Heart Association.

AMERICAN HEART ASSOCIATION RESEARCH GRANTS-IN-AID

Applications for Research Grant-In-Aid for 1954-1955 must be received not later than December 1, 1953. Information booklets and application blanks may be obtained from the Medical Director.

ANNUAL MEETING OF THE AHA, 1954

The Annual Meeting of the American Heart Association in 1954 will be held at the Conrad Hilton Hotel in **Chicago.** The Assembly Panels and the General Assembly will be held on Thursday and Friday, April 1 and 2, and will be followed by a specific scientific program on clinical cardiology on Saturday and Sunday, April 3 and 4, conducted under the auspices of the newly formed Section on Clinical Cardiology of the Scientific Council. These sessions will immediately precede the annual meeting of the American College of Physicians.

SCIENTIFIC PROGRAM OF THE SECTION ON CLINICAL CARDIOLOGY 1954

The Section on Clinical Cardiology of the American Heart Association will sponsor a two-day scientific program at the Conrad Hilton Hotel in Chicago on April 3 and 4, 1954. This program will constitute a portion of the Annual Meeting of the American Heart Association and immediately precedes the Annual Sessions of the American College of Physicians. The meeting will be open to all members of the medical profession. Doctor Wright R. Adams of Chicago is Chairman of the Program Committee. Members of the American Heart Association who wish to present papers should send a 250-300 word abstract of the proposed paper to Doctor Charles D. Marple, Medical Director, American Heart Association, Inc., 44 East 23rd Street, New York 10, New York. *All papers should be on subjects of distinct clinical interest. The deadline for the receipt of abstracts is January 1, 1954.*

ANNUAL SCIENTIFIC SESSIONS, 1954, and THE SECOND INTERNATIONAL CONGRESS OF CARDIOLOGY

The 27th Scientific Sessions of the American Heart Association will *not* be held at the usual time in 1954, but will take place following the 2nd International Congress of Cardiology in September. The International Congress of Cardiology will be held in **Washington, D. C.,** September 12 through 15, 1954, and the Scientific Sessions of the American Heart Association will also be held in Washington, September 16 through 19.